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Theophylline and Guaifenesin Capsules

» Theophylline and Guaifenesin Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of anhydrous theophylline ($C_7H_8N_4O_2$) and guaifenesin ($C_{10}H_{14}O_4$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Guaifenesin RS
USP Theophylline RS

Identification—Transfer a quantity of the contents of the Capsules, equivalent to about 150 mg of theophylline, to a separator, and add 15 mL of water. To a second separator transfer 15 mL of an aqueous Standard solution containing USP Theophylline RS and USP Guaifenesin RS corresponding, proportionately, to the amounts of theophylline and guaifenesin in the Capsules and having a known concentration of about 10 mg of theophylline per mL. Treat the contents of each separator as follows. Add 25 mL of chloroform, and shake vigorously for 0.5 minute. Allow the layers to separate, filter the lower chloroform layer through glass wool, and evaporate the filtrate to dryness. Dissolve the residue in 10 mL of chloroform. Apply separately 10 µL of each solution so obtained to a thin-layer chromatographic cellulose sheet with fluorescent indicator (see *Chromatography* ⟨621⟩), allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of methanol and water (95:5) until the solvent front has moved about 10 cm above the starting line. Remove the sheet from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Expose the sheet to short-wavelength UV light: the R_F values of the spots obtained from the test preparation correspond to those obtained from the Standard solution.

Dissolution ⟨711⟩—

Medium: simulated gastric fluid; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Procedure—Determine the amounts of theophylline ($C_7H_8N_4O_2$) and guaifenesin ($C_{10}H_{14}O_4$) dissolved in filtered portions of the solution under test and employing the procedure set forth in the *Assay*, making any necessary volumetric adjustments, in comparison with Standard solutions having known concentrations of USP Theophylline RS and USP Guaifenesin RS in the same medium.

Tolerances—Not less than 75% *(Q)* of the labeled amounts of $C_7H_8N_4O_2$ and $C_{10}H_{14}O_4$ are dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

pH 6.5 buffer solution—Dissolve 1.36 g of monobasic potassium phosphate in water to make 1000 mL. Carefully adjust with 2.5 N sodium hydroxide to a pH of 6.5, and filter.

Mobile phase—Prepare a degassed solution of *pH 6.5 buffer solution* and methanol (70:30).

Internal standard solution—Dissolve about 400 mg of caffeine in 1000 mL of a solution of methanol and water (90:10), and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Theophylline RS in *pH 6.5 buffer solution*, and dilute quantitatively with *pH 6.5 buffer solution* to obtain a solution (*Solution T*) having a known concentration of about 900*J* µg per mL, in which *J* is the ratio of the labeled amount of theophylline to that of guaifenesin. Transfer about 90 mg of USP Guaifenesin RS, accurately weighed, to a 200-mL volumetric flask, add about 150 mL of *pH 6.5 buffer solution*, shake to dissolve, dilute with *pH 6.5 buffer solution* to volume, and mix. Pipet 10 mL of this solution, 10 mL of *Internal standard solution*, and 5 mL of *Solution T* into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain a *Standard preparation* having known concentrations of about 90 µg of guaifenesin and about 90*J* µg of theophylline per mL.

Assay preparation—Transfer a number of Capsules, equivalent to about 900 mg of guaifenesin, to a 200-mL volumetric flask, add about 160 mL of *pH 6.5 buffer solution*, heat to dissolve completely, cool to room temperature, dilute with *pH 6.5 buffer solution* to volume, and mix. Dilute 10.0 mL of this solution with *pH 6.5 buffer solution* to 100.0 mL. Pipet 10 mL of the diluted solution and 10 mL of *Internal standard solution* into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.0 mL per minute. Chromatograph six replicate injections of the *Standard*

preparation, and record the peak responses as directed for *Procedure:* the relative standard deviation of the ratio of peak responses (peak response of ingredient/peak response of internal standard) is not more than 2.0% for theophylline and not more than 2.5% for guaifenesin. The resolution, *R,* between theophylline and caffeine is not less than 3.0.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.7 for theophylline, 1.0 for caffeine, and 1.5 for guaifenesin. Calculate the quantities, in mg, of anhydrous theophylline ($C_7H_8N_4O_2$) and guaifenesin ($C_{10}H_{14}O_4$) in the portion of Capsules taken by the formula:

$$10C(R_U/R_S)$$

in which C is the concentration, in µg per mL, of the appropriate USP Reference Standard in the *Standard preparation*, and R_U and R_S are the ratios of the peak responses of the corresponding analyte to those of caffeine in the *Assay preparation* and the *Standard preparation*, respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
THEOPHYLLINE AND GUAIFENESIN CAPSULES	Documentary Standards Support	SM52020 Small Molecules 5
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM52020 Small Molecules 5

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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